other post-prolyl cleaving enzymes. For Example, IgA 1 proteases recognize the cleavage site Ser-Thr-Pro-Pro-X (SEQ ID NO.6), (where X is any amino acid). Accordingly, Ser-Thr-Pro-Pro-R^1 (SEQ ID NO.7), is suitable for selectively binding to, and forming a complex with a functional group in the active site of an IgA 1 protease. The Ser-Thr in this targeting moiety may be readily substituted with any of the 20 naturally occurring amino acids, most preferably those having non-bulky side groups, such as Ala and Gly. It also is possible to substitute non-naturally occurring amino acids, such as 2-azetidinecarboxylic acid or pipecolic acid (which have 6-membered, and 4-membered ring structures respectively) for either of the Pro residues. Those skilled in the art will recognize that there are other such changes which can be made without significantly affecting the binding and complex forming character of these compounds.

Please replace the paragraph on page 18d, starting at line 14, with the following paragraph:

In the case of IgA 2, protease, the cleavage site in the natural substrate is Pro-Thr-Pro-X (SEQ ID NO.8), with hydrolysis occurring between Pro and X. Thus, a preferred P^1 R^1 binding moiety for binding to an IgA 2 protease has the formula Pro-Thr-Pro-R^1 (SEQ ID NO.9). Thr can be substituted by any of the naturally occurring amino acids, especially ones having non-bulky side groups, such as Ala, Gly or Ser. Other examples of post-prolyl cleaving enzymes which can be targeted by the targeting moieties of the invention include other IgA enzymes, encephalon degrading enzymes, vasopressin degrading enzymes, and oxytocin degrading enzymes.

Please replace the paragraph on page 32, starting at line 10, with the following paragraph:

2. Heterobivalent Compounds: General Structure

The heterobivalent compounds and agents taught herein may begin with the following general diagram as shown in Fig. 2A, the general formula for a heterobivalent compound. Figs. 2A- 2C are diagrams showing the general formula of several preferred

heterobivalent compounds: Fig. 2A is a diagram of a general heterobivalent template; Fig. 2B is a diagram of a heterobivalent example coupling a binding moiety to an MCC peptide (94-103) using a compatible linker, e.g., an AAAAAA (SEQ ID NO.1), linker group where A is L-alanine or D-alanine; and Fig. 2C is a diagram of a heterobivalent example coupling a binding moiety to a PLP peptide (139-151) using a comptabile linker, e.g., an AAAAAA (SEQ ID NO.1), linker group where A is L-alanine or D-alanine.

Please replace the paragraph on page 60, starting at line 11, with the following paragraph:

In the case of PLP, the heteordimer was constructed as HSLGKWLGHPDKFAAAAAA-εKbP (SEQ ID NO.3), where HSLGKWLGHPDKF (SEQ ID NO.2), was PLP 139-151, AAAAAA (SEQ ID NO.1), was a linker comprised of 6 alanines and εKbp was Lysine-boroProline in which the ε-amino of Lysine is covalently attached to the –COOH terminus of HSLGWLGHPDKFAAAAAA (SEQ ID NO.3). The first synthetic step was to order a custom peptide from a synthetic peptide lab. Using long established protocols, the peptide was built from the C-terminus staring with alanine which was immobilized on a resin. Sequentially AAAAAFKDPHGLWKGLSH (SEQ ID NO.4), were added using protected amino acids. The peptide was then removed from the resin to give a free –COOH terminus which could be reacted to form a peptide bond. The other residues HSLGKWLGHPDKFAAAAA (SEQ ID NO.5), were unreactive owing to protecting groups. Lysine-boroProline in which the α-NH_2 of Lysine was protected, the $B(OH)_2$ of boro Proline was protected with pinanediol, and the ε-NH_2 of Lysine was free was coupled to the peptide. The coupling was a peptide bond (-(C=0)-NH-) formed by standard peptide chemistry techniques. The result was then deprotected to yield the final product.

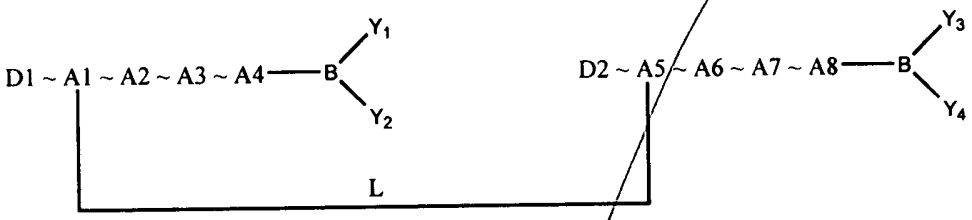
On a new page, immediately before the claims, please insert the attached Sequence Listing.

none submitted?

In the claims:

Please amend the claims as indicated below. For the convenience of the Examiner, a copy of the complete set of pending claims, in the form that they will take after entrance of the present Amendment, is included herewith as Appendix B.

1. (Amended) A compound, having the structure



wherein D1 and D2, independently, are selected from the group consisting of NH and NH_2,

wherein N represents any isotope of nitrogen,

wherein H represents any isotope of hydrogen;

"~", independently, is selected from the group consisting of a single bond and a double bond;

B represents, independently, any isotope of boron;

A1 and A5 are, independently, selected from a group consisting of a C, a CX moiety and an N,

wherein C represents any isotope of carbon,

wherein X represents any atom capable of forming a single bond with C;

each A2, A3, A4, A6, A7, and A8 are, independently, selected from a group consisting of a CX moiety, a CXZ moiety, a CZ moiety, an NX moiety, and an O,

wherein X and Z, are, independently, selected from the groups consisting of any atom capable of forming a single bond and any atom capable of forming a double bond with C or N and wherein O represents any isotope of oxygen;

wherein each Y1, Y2, Y3, and Y4 are, independently, selected from the group consisting of hydroxyl moiety and any reactive moiety that converts to a hydroxyl group moiety under

physiologic conditions; and

L represents a linker [molecule] moiety

(i) having a molecular weight ranging between about 100 daltons and about 2000 daltons,

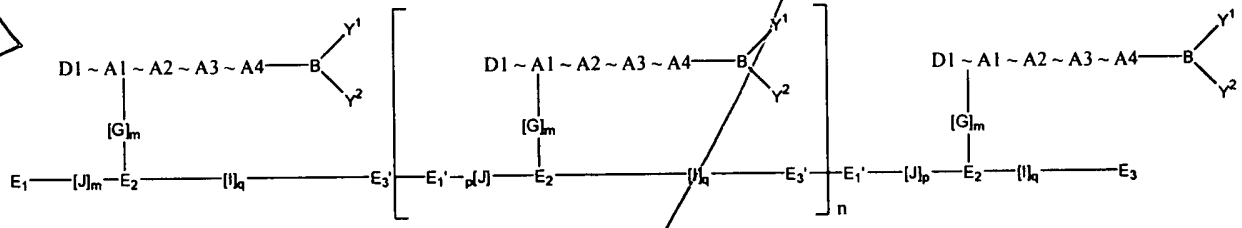
(ii) having a span ranging from about 20 Å to about 300 Å, and

(iii) containing a chain of atoms selected from the group consisting of a combination of C, O, N, S, and P [Ph] atoms, connected by single bonds or by double bonds in a manner that does not violate the laws of chemistry and wherein S represents any isotope of sulfur and P [Ph] represents any isotope of [phophorous] phosphorous.

Please cancel claims 17, 35, 39, 71, and 72.

Please add the following new claims:

--73. A compound, having the structure



wherein D is, independently, selected from the group consisting of NH and NH_2,

wherein N represents any isotope of nitrogen,

wherein H represents any isotope of hydrogen;

"~", independently, is selected from the group consisting of a single bond and a double bond;

B represents, independently, any isotope of boron;

A1 is, independently, selected from the group consisting of a C, a CX moiety, and an N,

wherein C represents any isotope of carbon,

wherein X represents any atom capable of forming a single bond with C;

each A2, A3, and A4 are, independently, selected from the group consisting of a CX moiety, a CXZ moiety, a CZ moiety, an NX moiety, and an O,

wherein X and Z, independently, are selected from the group consisting of any atom capable of forming a single bond and any atom capable of forming a double bond with C or N and wherein O represents any isotope of oxygen;

wherein Y1 and Y2 are, independently, selected from the group consisting of a hydroxyl moiety and any reactive moiety that converts to a hydroxyl group moiety under physiological conditions;

n represents an integer between 1 and 200, inclusive;

wherein E1 and E3 are independently selected from the group consisting of a carboxylate, amino, imidazole, sulfhydryl, aldehyde, ester, amide, acid chloride, carbonate, and carbamate group such that the E1 and E3 are capable of reacting and forming an –E1'—E3'— adduct with a covalent bond between E1' and E3';

wherein $[J]_p$, $[I]_q$, and $[G]_m$ together comprise a linker moiety, and wherein $[G]_m$, $[J]_p$, and $[I]_q$ represent, independently, a linker group (i) having a molecular weight ranging between about 100 daltons and about 2000 daltons, (ii) having a span ranging from about 20 Å to about 300 Å, and (iii) containing a chain of atoms selected from the group consisting of a combination of C, O, N, S, and P atoms, connected by single bonds, double bonds, or triple bonds in a manner that does not violate the laws of chemistry and wherein S represents any isotope of sulfur and P represents any isotope of phosphorus; and wherein m, p, and q represent, independently, an integer from 1 to 50, inclusive;

E2 is selected from the group consisting of CX, CH, N, PYZ, PU, and B such that E2 is capable of forming a covalent bond with $[J]_p$, $[G]_m$, and $[I]_q$ and

wherein C is any isotope of carbon;

X is, independently, selected from the group consisting of any atom capable of forming a single bond with carbon;

Y is, independently, selected from the group consisting of any atom capable of forming a single bond with phosphorous;

Z is, independently, selected from the group consisting of any atom capable of forming a single bond with phosphorous;

H is any isotope of hydrogen;

N is any isotope of nitrogen;

P is any isotope of phosphorus;

B is an isotope of boron;

U is, independently, selected from the group consisting of any atom capable of forming a double bond with phosphorous.--

Remarks

The Specification has been amended to include the SEQ ID NOs where appropriate as requested by the Examiner. An amended Sequence Listing including all the sequences in the Specification is enclosed herein along with a computer readable copy of the Sequence Listing. Applicant submits that no new matter has been added to the Application by the amendment to the Sequence Listing and states that the paper copy and computer readable copy of the Sequence Listing are the same.

The IDS filed October 30, 2000 was submitted without copies of many of the cited references because copies of these references had been previously submitted to the Patent Office in prior application USSN 08/837,305 (now U.S. Patent 5,965,532), which the present application claims priority to under 35 U.S.C. § 120. The references cited in the prior application were marked with an asterisk next to the citation on the Form PTO-1449. This was noted on page 4 of the Statement under 37 CFR §§ 1.56, 1.97, and 1.98 that was submitted as part of the IDS. For the convenience of the Examiner, Applicant has included another copy of the IDS submission of October 30, 2000, and Applicant requests that Examiner consider the listed references and return the initialed Form PTO-1449 listing the references with the next Office Action.

Claims 1, 17, 35, 39, 71 and 72 are pending in the application. Claims 17, 39, 71, and 72 have been withdrawn from consideration. Claims 1 and 35 stand rejected. Claim 1 is amended